

REMARKS

The foregoing amendment to the specification is supported in Figure 2A as originally filed and does not introduce new matter.

The amendment to Figure 2A merely adds a sequence identifier to the figure to comply with 37 C.F.R. 1.821(d) and does not introduce new matter.

Enclosed is a marked-up version of the changes made by this amendment. The enclosed pages are captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**"

Entry of the foregoing amendment is respectfully requested and favorable action on the merits is earnestly solicited.

Date: December 4, 2002

Respectfully submitted,

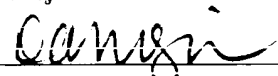

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CERTIFICATE OF MAILING UNDER 37 CFR 1.8

I hereby certify that this correspondence and its listed enclosures is being deposited with the United States Postal Service as First Class Mail, postage paid, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231 on **December 4, 2002**

Name: **Deborah A. Mojarro**

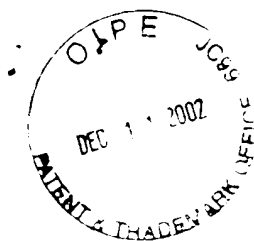
Signed: 

Date: 12/4/02

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Page 8, lines 12-15 have been amended as follows:

Figure 2A-2B shows design of the targeting construct used to disrupt nuclear hormone receptor genes. Figure 2A, which illustrates the target sequence (SEQ ID NO:1) for the targeting construct, shows the location and extent of the disrupted portion of the nuclear hormone receptor gene, as well as the nucleotide sequences flanking the Neo' insert in the targeting construct. Figure 2B shows the sequences identified as SEQ ID NO:3 and SEQ ID NO:4, which were used as the targeting arms (homologous sequences) in the nuclear hormone receptor targeting construct.



Construct

GI Number(s): 2267577

Gene Family: Nuclear Hormone Receptor

Gene

Subfamily: Orphan NHR

Gene Sequence: full-length cDNA, Mouse

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

CCCTCGACCTCGAGATCCATTGTGCTCTAAAGCAGAGTCTGGGTCTACCTACATATGGC
ACCGAGGATACCTAGAGGCCCATGCAAGAGAAGGCCCTTGTCTTCCAGGCACTGAGGAC
CFCAGTCCCTAATTCCCTGGCACTTCCCTGAGATCTCAAGGAAAGCAGGGTCAAGCAGGAGG
CCTGGGGAGAGGAGGCATCCTACACCCAAATCTTGTGGCCTCCCTCCCTAAGGSAACAGGA
GACCATGACAGCTATGCTAACACTAGAAACCATGGCCAGTGAAGAAGAATATGGGCCCGAG
GAATCTGTGGGGTGTGGAGATGGGGCCACAGGCTATCATTTCCACGCCCTGACTTGTGA
GGGTGGAGGGCTTCTTCAGACGGAACATCAGCAAAACCATTTGGTCCCATCTGTCCCGTT
TCTCTGGAAGGTGTGAGGTCAGCAAGGCCAGAGACGCCACTGTCCAGCCTGAGGTTGCA
GAAGTGTCTAAATGTGGGCATGAGGAAABACATGATACTGTGAGCAGAAGCCTCTGGCATT
GCGGCGAGCCAGACAGGCACAGCGSCGGGCAGAGAAAGCATCTTTGCAACTGAATCAGCA
GCAGAAAGAACTGGTCCAGATCCTCTGGGGGCCACACTCGCCATGTGGGCCCATTTGTT
TGACCAAGTTTGTGCAAGTTCAGGCCCTCAGCCCTATCTGTTTCATGCATCACCGGCCCTTTCCA
GCTCTGGGGGCCCGTGTGCTCTGCTCACACACTTTGCAGATATCAACACGTTTATGGT
GCAACAGATCATCAAGTTCACCAAGGATCTGCGGCTCTTCCGGTCCCTAACCATGGAGGA
CCAGATCTCCCTTCTCAAGGGAGCGGCTGTGGAAATATGTCATATCTCACTCAACACTAC
CTTCTGTCTTCAAACAGAGAATTTCTTCTGTGGGCTCTTTGCTACAAGATGGAGGACGC
AGTCCATGCAAGGTTCAGATACGAGTTTGTGGAGTCGATCCTCCACTTCCATAAAAAACCT
GAAAGGACTGCATCTCCAGGAGCCTGAGTATGTGCTCATGGCTGCCACGGGCCCTCTTCTC
CCCTGGTTTCTGTATGCAAAGCTGATGGGCCTGCTGGCTGACCTCCGGAGTATAAACAAT
GCATACTCCTATGAACCTCAGCGCTTGGAGGAAGTGTCTGCTATGACGCCGCTGCTCGGG
GAGATTTGCAGTTGAGGCCCAGGCTTGCACTCTTCCCCAGACCCCCAGGGATACACTGG
CCTGGAAAGGTTACAGCGCTGGACCCCCACACAGCAGAAGGAGCTTGGGAGTGGCAATGAA
ATGCTGAACAGT

Gene Sequence
Structure *

282 bp

Sequence Deleted

403 bp

Size of full-length
cDNA: 1332 bp

FIG. 2A



Construct

GI Number(s): 2267577

Gene Family: Nuclear Hormone Receptor

Gene Subfamily: Orphan NHR

Gene Sequence: full-length cDNA, Mouse

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

```
CCCTCGACCTCGAGATCCATTGTGCTCTAAAGCAGAGTCTGGGTCCTACCTACATATGGC
ACCGAGGATACCTAGAGGCCCATGCAAGAGAAGGCCCTTGTTTTCCAGGCACTGAGGAC
CGCAGTCCCTAATTCCTGGCAGTTCCCTGAGATCTCAAGGAAAGCAGGGTCAGCGAGGAGG
CCTGGGGAGAGGAGGCATCCTACACCCAATCTTGTGGCCTGCTGCCTAAGGGAAACAGGA
CAACATCACACCTATCTTACACTAGAACCATGGCCAGTCAAGCAAGATATGGGCGAG
GAACCTGTGTGGTGTGTGGAGACCGGGCCACAGGCTATCATTTCCACGCCCTGACTTGTGA
GGGCTGCAAGGGGTTTCTTCAGACGAACAGTCAGCAAAACCATTTGCTCCCATCTGTCCGTT
TGCTGGAAGGTGTGAGGTCAAGCAAGGCCUAGAGACGUCACCTGTCCAGCCTGCAGSTTGA
GAAGTGTCTAAADGTTGGCATGAGSAAAGACATGATACTGTCAGCAGAAGCCCTGGCATT
GCGGCGAGCCAGACAGGCACAGCGGCGGGCAGAGAAAGCATCTTTGCAACTGAATCAGCA
GCAGAAAGAACTGGTCCAGATCCTCCTGGGGGCCACACTCGCCATGTGGGGCCATTGTT
TGACCAAGTTTGTGCAGTTCAAGCCTCCAGCCTATCTGTTTCATGCATCACCGGCCTTTCCA
GCCTCGGGGCCCCGTGTTGCCTCTGCTCACACACTTTGCAGATATCAACACGTTTATGGT
GCAACAGATCATCAAGTTCACCAAGGATCTGCCGCTCTTCCGGTCCCTAACCATGGAGGA
CCAGATCTCCCTTCTCAAGGGAGCGGCTGTGGAAATATTGCATATCTCACTCAACACTAC
GTTCTGTCTTCAAACAGAGAATTTCTTCTGTGGGCCTCTTTGCTACAAGATGGAGGACGC
AGTCCATGCAGGGTTCCAGTACGAGTTTTTGGAGTCGATCCTCCACTTCCATAAAAACCT
GAAAGGACTGCATCTCCAGGAGCCTGAGTATGTGCTCATGGCTGCCACGGCCCTCTTCTC
CCCTGGTTTCTGTATGCAAAGCTGATGGGCCTGCTGGCTGACCTCCGGAGTATAAAACAAT
GCATACTCCTATGAACCTCAGCGCTTGGAGGAACCTGTCTGCTATGACGCCGCTGCTCGGG
GAGATTTGCAGTTGAGGCCCAGGCTTGATCCTTTCCCCAGACCCCCAGGGATACACTGG
CCTGGAAAGGTTACAGCGCTGGACCCACACAGCAGAAGGAGCTTGGGAGTGGCAATGAA
ATGCTGAACAGT (SEQ ID NO:1)
```

Gene Sequence
Structure *

282 bp

Sequence Deleted

403 bp

Size of full-length
cDNA: 1332 bp



FIG. 2A